Modeling of the thermodilution curve for coronary flow assessment

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The coronary circulation supplies the heart with blood. Every time the heart beats, about 5 percent of the stroke volume goes to the coronary arteries. In a resting situation, when the cardiac output is about 4.5 l/min, this yields an average coronary blood flow of 225 ml/min [1]. When a coronary artery is stenosed, the flow through that artery will decrease, depending on the severity of the stenosis. Since intervention by Percutane Transluminal Coronary Angioplasty (PTCA) or bypass surgery in order to revascularize the coronary circulation should only be performed in severe cases, it is important to be able to accurately determine coronary blood flow in order to diagnose the severity of a stenosis.

Methods to indicate the degree of decreased blood flow, are the assessment of the Coronary Flow Reserve (CFR) and the Fractional Flow Reserve (FFR) [2]. The CFR gives the ratio between flow during maximum vasodilation (hyperemic flow) and flow in rest (baseline flow). The FFR is the ratio between maximum flow in the stenosed artery and the maximum flow in a healthy artery. Both ratios are used to determine the hemodynamical state of the artery and the peripheral vascular bed.

To determine the flow in an artery, the method of thermodilution can be used. This method uses a bolus injection of cold saline into the bloodstream and measures the temperature change at a location distal of the injection. An example of the kind of temperature profile which is being measured, is pictured below. This curve, where the measured temperature is plotted against the time, is called a thermodilution curve (figure 1.1).

*figure 1.1: The thermodilution curve (data from N.H.J. Pijls, used with permission)*
If the saline injection and the thermodilution curve would be simple delta-functions, the flow velocity would be derived by dividing the traveled distance of the saline by the time taken to travel that distance. Since the curve is not a delta-function, a mean transit time, $T_{mn}$, is introduced. $T_{mn}$ is the averaged time it takes for the cold saline to travel from the point of injection to the point of temperature measurement. $T_{mn}$ is calculated using [2]:

$$
T_{mn} = \frac{\int_{\infty}^{\infty} t \Delta T(t) dt}{\int_{0}^{\infty} \Delta T(t) dt}
$$

(1.1)

Here $\Delta T(t)$ represents the temperature drop at a given $t$. From $T_{mn}$ and the location of the temperature measurement the flow velocity can be determined.

The goal of this study is to model the thermodilution curve. This is done in order to be able to assess the blood flow more precise and to come to an automatic flow detection algorithm.

In chapter 2 the methods used to model the thermodilution curve are explained. After an introduction, the first part of the model is presented. Here the mixing of the cold saline with the blood in front of the entrance to the coronary artery is represented by a mixing chamber. The resulting mixture then travels into the coronary artery. The artery is modeled as a tube in section 2.3 and the effects on the temperature by diffusion, convection and heat exchange through the wall are calculated using equations for conservation of mass and energy. The resulting thermodilution equation is then solved in section 2.4. Chapter 3 contains the results and the report is concluded in chapter 4.
2 Methods

2.1 Introduction

In order to model the thermodilution curve, two compartments are defined [3]. The first compartment is the actual injection of the cold saline into the blood. The saline is injected through a catheter which ends just in front of the aortic valve and the entrance to the right or left coronary arteries. Here the saline is assumed to be mixed with the blood before this mixture travels into the second compartment of the model, the coronary artery.

In the coronary artery, the mixture of saline and blood travels from the entrance of the artery, past the temperature measuring location and further into the coronary branches.

2.2 The mixing chamber

The location where the cold saline is injected is referred to as the mixing chamber. Here the saline mixes with the blood and this mixture enters the coronary artery. The mixing chamber is defined as depicted in figure 2.1:

\[ q_b = \text{blood flow} \]
\[ q_s = \text{saline flow} \]
\[ q_a = \text{flow to aorta} \]
\[ q_0 = \text{flow to coronary artery} \]
\[ T_b = \text{blood temperature} \]
\[ T_s = \text{saline temperature} \]
\[ T_0 = \text{mixture temperature} \]
\[ V_m = \text{volume of the mixing area} \]

Compliance of the mixing chamber is neglected, so mass conservation requires:

\[ q_b + q_s = q_a + q_0 \]  \hspace{1cm} (2.1)\]

For constant and equal density and constant and equal specific heat at constant pressure for both blood and saline, the heat equation is:
\[
V_m \frac{dT_0}{dt} = q_a T_b + q_s T_s - q_a T_o - q_o T_o
\]  
(2.2)

rearranging and dividing by \( V_m \) gives:

\[
\frac{dT_0}{dt} + \frac{q_s + q_o}{V_m} T_0 = \frac{q_a T_b + q_s T_s}{V_m}
\]  
(2.3)

To obtain \( T_0 \), the general solution for a first order differential equation is used:

if \( y' + p(x)y = r(x) \)
then \( y(x) = e^{-\int p(x)dx} \left[ \int e^{\int p(x)dx}r(x)dx + c \right] \), with \( h = \int p(x)dx \)

For the mixing chamber differential equation this yields, with \( T_0(0) = T_b \):

\[
T_0 = e^{\int q_s + q_o t dt} \left[ \int e^{\int q_s + q_o t dt} \left( \frac{q_a T_b + q_s T_s}{V_m} \right) dt + T_b \right]
\]  
(2.4)

If the saline injection is a single square wave that begins at \( t = 0 \) and ends at \( t = 4 \) (figure 2.2), then the corresponding temperature profile, based on the given parameter values, is depicted in figure 2.3. Here, a steady case is assumed.

*figure 2.2: The input flows; the injection is represented by the solid line.*
The output temperature $T_0$ will be the input temperature for the second compartment of the model, which is the coronary artery.
2.3 The tube

The temperature of the mixture, while traveling through the coronary artery, changes over time due to heat convection, diffusion and heat exchange at the wall. These factors are used to calculate the change in temperature of the mixture over a certain distance and time in an artery.

To simplify the problem, the artery is defined as a tube with specifications as given in figure 2.4.

\[
\text{with: } u_z = \text{velocity in } z\text{-direction} \\
R = \text{tube radius} \\
d = \text{wall thickness}
\]

\textit{figure 2.4: Definition of the tube}

2.3.1 Conservation equations

To calculate the change in temperature, conservation equations for energy and mass are needed. The energy equation without internal heat production and viscous dissipation using cylindrical coordinates is defined as:

\[
\rho c_p \left( \frac{\partial T}{\partial t} + u_r \frac{\partial T}{\partial r} + u_\theta \frac{\partial T}{\partial \theta} + u_z \frac{\partial T}{\partial z} \right) = \lambda \left[ \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2 T}{\partial \theta^2} + \frac{\partial^2 T}{\partial z^2} \right]
\]  

(2.5)

with blood density \( \rho \), heat capacity of blood \( c_p \) and heat diffusion coefficient of blood \( \lambda \).

The mass conservation equation is defined as:

\[
\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \vec{v}) = 0
\]

(2.6)

Blood is assumed to be incompressible, so \( \frac{\partial \rho}{\partial t} = 0 \) and \( \nabla \rho = 0 \). This leads to

\[
\nabla \cdot \vec{v} = 0
\]

(2.7)
Written in cylindrical coordinates this gives:

\[
\nabla \cdot \mathbf{v} = \frac{1}{r} \frac{\partial}{\partial r} (ru_r) + \frac{1}{r} \frac{\partial u_\theta}{\partial \theta} + \frac{\partial u_z}{\partial z} = 0
\]

(2.8)

Because fully developed flow is assumed, the velocities that are not in the direction of the longitudinal axis of the tube are zero: \(u_r = u_\theta = 0\), so from (2.8): \(\frac{\partial u_z}{\partial z} = 0\).

Substituting this into the energy equation (2.5) gives:

\[
\frac{\partial T}{\partial t} + \dot{u} \frac{\partial T}{\partial z} - a \frac{\partial^2 T}{\partial z^2} - a \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T}{\partial r} \right) = 0, \quad \text{for } 0 \leq r \leq R
\]

(2.9)

with: \(a = \frac{\lambda}{\rho c_p}\), the heat equalizing coefficient for blood.

### 2.3.2 Heat balance for the wall

When using (2.9) to determine the temperature profile in the wall of the tube, the heat diffusion in \(z\)-direction can be neglected, because \(\frac{\partial T}{\partial z} \ll \frac{\partial T}{\partial r}\) in the wall.

This leads to the following equation for the heat balance in the wall:

\[
\frac{\partial T}{\partial t} - a_w \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T}{\partial r} \right) = 0, \quad \text{for } R < r \leq R + d
\]

(2.10)

with \(a_w\) the heat equalizing coefficient of the wall.

If the penetration depth of the heat in the wall is much smaller then the wall thickness, then the term \(\frac{\partial T}{\partial t}\) is zero. Since \(a_w\) is constant this leads to:

\[
\frac{1}{r} \frac{d}{dr} \left( r \frac{dT}{dr} \right) = 0
\]

(2.11)

Integration of (2.11) with \(R+d\) as the outer wall diameter, where \(T\) is the body temperature (\(= T_b\)), and \(R\) as the inner wall diameter, where \(T = T_R\):

\[
T(r) = T_b + (T_R - T_b) \frac{\ln r - \ln(R + d)}{\ln R - \ln(R + d)}
\]

(2.12)

with:

- \(T(r)\) = temperature in radial direction
- \(T_b\) = temperature on the outside of the wall
- \(T_R\) = temperature on the inside of the wall
- \(d\) = wall thickness

Taking the derivative of (2.12) gives the term:
\[
\frac{\partial T(r)}{\partial r} = \frac{T_R - T_b}{\ln R - \ln(R + d)} r
\]

which can be used in (2.9).

### 2.3.3 Thermodilution equation

Integrating (2.9) over a radial slice now gives:

\[
2\pi \int_0^R \frac{\partial T}{\partial r} r dr + 2\pi u_z \int_0^R \frac{\partial T}{\partial z} r dr - 2\pi a \int_0^R \frac{\partial^2 T}{\partial z^2} r dr - 2\pi a \int_0^R \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial T}{\partial r}\right) r dr = 0
\]

(2.14)

\[
\pi R^2 \frac{\partial T}{\partial t} + \pi u_z R^2 \frac{\partial T}{\partial z} - \pi a R^2 \frac{\partial^2 T}{\partial z^2} - 2\pi a \frac{T - T_b}{\ln R - \ln(R + d)} = 0
\]

(2.15)

divide by \( \pi R^2 \):

\[
\frac{\partial T}{\partial t} + u_z \frac{\partial T}{\partial z} - a \frac{\partial^2 T}{\partial z^2} - 2a \frac{T - T_b}{\ln R - \ln(R + d)} \frac{1}{R^2} = 0
\]

(2.16)

Now define \( \varepsilon \) as:

\[
\varepsilon = -\frac{2a}{R^2} \frac{1}{\ln R - \ln(R + d)} = \frac{\lambda}{\rho c_p R^2} \frac{2}{\ln(1 + \frac{R}{d})}
\]

(2.17)

and since \( u_z \) is a constant and corresponds with the constant flow \( q_0 \) as defined in the mixing chamber, \( u_z = \frac{q_0}{A} \). Here \( A \) is the cross-sectional area of the tube.

The equation for the temperature change, or thermodilution equation, becomes:

\[
\frac{\partial T}{\partial t} + \frac{q_0}{A} \frac{\partial T}{\partial z} - a \frac{\partial^2 T}{\partial z^2} + \varepsilon(T - T_b) = 0, \quad \text{for } z > 0, \ t > 0
\]

(2.18)
2.4 Solution of the problem

2.4.1 Problem definition

In section 2.3.3 the thermodilution equation is defined as:

$$\frac{\partial T}{\partial t} + \frac{q_0}{A} \frac{\partial T}{\partial z} - a \frac{\partial^2 T}{\partial z^2} + \varepsilon (T - T_b) = 0, \text{for } z > 0, \ t > 0$$  \hspace{1cm} (2.19)

To solve this equation an initial condition at $t = 0$ can be specified:

$$T(z, 0) = T_b$$  \hspace{1cm} (2.20)

and the mixing chamber's output temperature, $T_0$ in section 2.2, is the boundary condition for $z = 0$:

$$T(0, t) = F(t) = e^{-\int_0^t \frac{q_0 + q_b}{V_m} \ dt} \left[ \int_0^t e^{\int_0^v \left( \frac{q_0 T_b + q_z T_z}{V_m} \right) \ dt} + T_b \right]$$  \hspace{1cm} (2.21)

It is convenient to scale (2.19), in order to simplify the problem.

2.4.2 Scaling

$T, t$ and $z$ are the variables that need to be made dimensionless, since all others are constants. They are made dimensionless using:

$$T' = \frac{T - T_b}{T_b - T_s}$$

$$t' = \frac{t}{t^*}$$

$$z' = \frac{z}{z^*}$$  \hspace{1cm} (2.22)

Substitute these in (2.19) and rearrange:

$$\frac{(T_b - T_s)}{t^*} \frac{\partial T'}{\partial t'} = \frac{a (T_b - T_s)}{z^*} \frac{\partial^2 T'}{\partial z'^2} - \frac{q_0 (T_b - T_s)}{z^* A} \frac{\partial T'}{\partial z'} - \varepsilon T' (T_b - T_s)$$  \hspace{1cm} (2.23)

divide by $\frac{(T_b - T_s)}{t^*}$ and substitute $t^* = \frac{1}{\varepsilon}$:

$$\frac{\partial T'}{\partial t'} = \frac{a}{\varepsilon z^*} \frac{\partial^2 T'}{\partial z'^2} - \frac{q_0}{\varepsilon z^* A} \frac{\partial T'}{\partial z'} - T'$$  \hspace{1cm} (2.24)
Now substitute $z^* = \frac{q_0}{A}$:

$$\frac{\partial T'}{\partial t'} = \frac{\varepsilon A^2 a}{q_0} \frac{\partial^2 T'}{\partial z'^2} - \frac{\partial T'}{\partial z'} - T'$$

(2.25)

And with $D_c = \frac{\varepsilon A^2 a}{q_0}$, the equation becomes:

$$\frac{\partial T'}{\partial t'} = D_c \frac{\partial^2 T'}{\partial z'^2} - \frac{\partial T'}{\partial z'} - T'$$

(2.26)

To simplify the use of the equation, the index (') is dropped and the dimensionless thermodilution equation becomes:

$$\frac{\partial T}{\partial t} = D_c \frac{\partial^2 T}{\partial z^2} - \frac{\partial T}{\partial z} - T$$

(2.27)

Since the terms in 2.27 are scaled and $O(1)$, the value of $D_c$ is evaluated using [3]:

$$\varepsilon = 0.111 \text{ \text{1/s}}$$

$$A = 7.1\text{e-6 m}^2$$

$$a = 1.4\text{e-7 m}^2/\text{s}$$

$$q_0 = 4\text{e-6 m}^3/\text{s}$$

$D_c$ has a value of approximately $4.8\text{e-8}$. This means it is possible to discard the second order term in 2.27:

$$\frac{\partial T}{\partial t} = -\frac{\partial T}{\partial z} - T$$

(2.28)

In order to solve (2.28) the variables $z$ and $t$ are made dimensionfull again using:

$$t^* = \frac{t}{t^*}, \text{ with } t^* = \frac{1}{\varepsilon}$$

and

$$z^* = \frac{z}{z^*}, \text{ with } z^* = \frac{q_0}{A}$$

It is convenient to leave $T$ dimensionless for now, but the index (') is reintroduced to be able to discern between the dimensionless $T'$ and dimensionfull $T$. Equation (2.28) now reads after rearranging:
\[
\frac{\partial T'}{\partial t} + \frac{q_0}{A} \frac{\partial T'}{\partial z} = -\varepsilon T'
\] (2.29)

To simplify this, the heat equalizing coefficient for the wall, \(\varepsilon\), is assumed zero. This leaves the linear advection equation:

\[
\frac{\partial T'}{\partial t} + \frac{q_0}{A} \frac{\partial T'}{\partial z} = 0
\] (2.30)

Substituting the dimensionless temperature \(T'\), according to \(T' = \frac{T - T_b}{T_k - T_s}\), into (2.30) only results in the loss of the accent:

\[
\frac{\partial T}{\partial t} + \frac{q_0}{A} \frac{\partial T}{\partial z} = 0
\] (2.31)

### 2.4.3 Solution

The solution of (2.31) can be obtained with the method of separating variables. Two new variables replace \(T(z,t)\) according to \(T(z,t) = X(z) \cdot Y(t)\). Substitution in (2.31) and rearranging yields:

\[
\frac{1}{Y} \frac{\partial Y}{\partial t} = -\frac{q_0}{AX} \frac{\partial X}{\partial z}
\] (2.32)

Equation (2.32) only holds if both sides of the equation are equal to the same constant. In this case the constant is defined as ‘\(k\)’ and two separate equations are obtained:

\[
1 \frac{\partial Y}{Y} = k \quad \text{and} \quad \frac{q_0}{AX} \frac{\partial X}{\partial z} = k
\] (2.33)

Solution of (2.33) and reintroduction of \(T(z,t)\) leads to:

\[
\ln(Y) = t \cdot k + C_1 \quad \text{and} \quad \ln(X) = -\frac{zA}{q_0} \cdot k + C_2
\] (2.34)

\[
Y(t) = e^{t \cdot k + C_1} \quad \text{and} \quad X(z) = e^{-\frac{zA}{q_0} \cdot k + C_2}
\] (2.35)

\[
T(z,t) = X(z) \cdot Y(t) = Ce^{k(t - \frac{zA}{q_0})}
\] (2.36)

The constants \(C\) and \(k\) can be solved using the initial and boundary conditions from (2.20) and (2.21).
Combining (2.20) and (2.36) leads to:

\[ T_b = Ce^{-\frac{zA}{q_0}} \Rightarrow C = \frac{T_b}{e^{-\frac{zA}{q_0}}} \]  

(2.37)

Combining (2.21) and (2.37) leads to:

\[ F(t) = Ce^{kt} \Rightarrow F(t) = T_b e^{k(t+\frac{zA}{q_0})} \Rightarrow k = \frac{\ln\left(\frac{F(t)}{T_b}\right)}{t + \frac{zA}{q_0}} \]  

(2.38)

Now the values for C and k can be substituted in (2.36):

\[ T(z, t) = T_b e^{\frac{\ln(F(t))}{t + \frac{zA}{q_0}}} \]  

(2.39)

or simplified:

\[ T(z, t) = F(t) \]  

(2.40)

with:

\[ F(t) = e^{-\int_0^{\frac{q_0}{V_m}} dt} \left[ e^{\int_0^{\frac{q_0}{V_m}} dt} \left( \frac{q_s T_b + q_s T_m}{V_m} \right) dt + T_b \right] \]  

(2.41)
3 Results

Using (2.40), temperatures can be calculated for any positive $z$ and $t$. This means that for a given distance from the entrance of the tube, a temperature profile can be obtained. An example is shown in figure 3.1, where $z = 5$ cm and the mixing chamber output from figure 2.3 is used as input.

![Figure 3.1: The thermodilution output temperature](image)

The profile that is obtained is almost exactly the same as that of the mixing chamber output. However, the profile does flatten slightly towards $37^\circ C$ for increasing measurement distances from the entrance of the tube.

Figure 3.2 shows the approximation of the patient data from figure 1.1 by the thermodilution model. The approximation was made by variation of the parameters from (2.40). Most of the parameters are known and they can be used to determine the two remaining unknown parameters. These unknown parameters that need to be adjusted to obtain a proper approximation are the coronary flow, $q_0$, and the mixing chamber control volume, $V_m$. The parameters used to fit the patient data in figure 3.2 are:

- $q_0 = 80$ ml/s
- $q_s = 40$ ml/s
- $q_a = 105$ ml/s
- $V_m = 80$ ml
- $T_b = 37^\circ C$
- $T_s = 20^\circ C$
\[ q_0 = 15 \text{ ml/s} \]
\[ V_m = 60 \text{ ml} \]

*figure 3.2: a thermodilution curve is fitted to patient data*
H4 Conclusions and discussion

A model was made to produce thermodilution curves. In the mixing chamber compartment of the model, the mixing of the injected cold saline with the blood is modeled. In the second compartment, the transport of the mixture through a tube is modeled, resulting in (2.18). The use of (2.4) as a boundary condition for solving (2.18) finally resulted in (2.40). This equation describes the temperature of the convected saline and blood mixture.

To be able to estimate coronary flow, several measurement specific parameters as used in (2.40) and (2.41) need to be defined. Using these parameters, a curve can be matched to patient data by adjusting the unknown coronary flow, $q_0$, and the mixing chamber control volume, $V_m$. However, this matching procedure needs to be further evaluated before it can be applied.

From the obtained thermodilution curves, it appears that patient data can be approximated with the current model. Whether the approximations yield usable values for the coronary flow has not been investigated in this study.

Also, the model was simplified to a linear advection problem, which probably reduces the accuracy of the estimation of the coronary flow. However, if the transport of the mixture can be described by a linear advection equation, then the input temperature profile at the entrance of the tube is highly defining for the final approximation of the thermodilution curve. This means that future work involving the thermodilution curve perhaps should concentrate on more advanced modeling of the saline injection curve as input for the mixing chamber in stead of the step function used in this report. This could result in better thermodilution curve approximations and consequently more accurate coronary flow calculations.
References

